REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claim Amendments

Claim 1 has been amended to delete the word "general", and to delete the brackets. Claim 1 has also been amended to limit R1 to Me, and to limit X to CHF.

Claim 6 has been amended to include a pharmaceutically acceptable auxiliary agent. Support for this amendment is found on page 13, lines 23-24 of Applicants' specification.

Claims 8 and 9 have been amended to recite methods of use, in order to better comply with U.S. practice.

Claims 2-5 and 7 have been cancelled, without prejudice.

No new matter has been added to the application by the above-discussed amendments.

Objection to Amendment Filed August 28, 2006

The objection to the Amendment filed August 28, 2006, as introducing new matter into the disclosure, is respectfully traversed.

The Examiner states that the changes made to paragraph [0071] on pages 34-35 add material which is not supported by the original disclosure.

Applicants respectfully disagree with the Examiner's assertion, since Fig. 1 of the application, which is referred to in amended paragraph [0071], supports the change from 10 mg/kg to 1 mg/kg. Additionally, as stated in the remarks in the Preliminary Amendment, this amendment is made to correct a typographical error.

Accordingly, the amendment changing 10 mg/kg to 1 mg/kg does not constitute new matter, and the above objection should be withdrawn.

Claim Objections

The objection to claims 7-9 for being substantial duplicates of claim 1 has been rendered moot by the above-discussed claim amendments.

Specifically, claim 7 has been cancelled, without prejudice, and claims 8 and 9 have been rewritten in method of use format.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-9 as being indefinite under 35 U.S.C. § 112, second paragraph has been rendered moot by the above-discussed claim amendments.

Specifically, the word "general" and the brackets have been deleted from claim 1. Further, amended claim 1 contains a period only at the end of the claim.

Patentability Arguments

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Rejection Under 35 U.S.C. § 103(a)

The rejection of claims 1, 2 and 5-9 under 35 U.S.C. § 103(a) as being unpatentable over Villhauer (U.S. 6,432,969) and Villhauer (WO 98/19998), taken alone or in combination with each other, is respectfully traversed.

As discussed above, Applicants have amended claim 1 to limit R1 to Me and X to CHF. Neither of the cited references teach or suggest the compound recited in Applicants' amended independent claim 1.

The Examiner broadly states that WO '998 generically describes compounds. However, Applicants assert that absent a more specific discussion regarding why the genus would render Applicants' claimed species obvious, the Examiner has not met his burden in establishing a *prima facie* case of obviousness.

Further, the Examiner states that the difference between the compounds of US '969 and Applicants' compounds is that of homology, (pentyl vs. butyl).

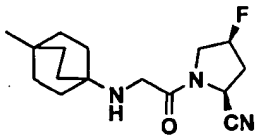
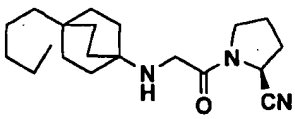
Applicants' claim 1 now requires that R1 is methyl, and X is CHF. Neither of the cited references, nor a combination thereof, teaches the compound recited in Applicants' amended claim 1.

The Examiner also takes the position that since both cited references teach pyrrolidine compounds that are structurally similar to each other and are useful in treating similar diseases/ disorders, that instantly claimed invention would have been obvious to one skilled in the art.

Applicants respectfully disagree. MPEP 716.02(a)(II) states that evidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. "Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness."

Although Applicants disagree that the Examiner has established a *prima* facie case of obviousness, the following comments are provided to expedite prosecution of this application. In order to compare the compound recited in amended claim 1 with the compound of US '969 (Example 2-DD), Applicants have conducted a test for the ability of these compounds to inhibit DPP-IV activity *in vitro* and *in vivo*. The results are shown in Table 1, below.

Table 1

	Structure	*In vitro*	*In vivo* Inhibition (%)
		IC_{50} (nM)	0.5h
Compound defined by the amended claim (Example 3)		0.25	100
Compound of Cited document (US6432969)		4.1	60

The *in vitro* test was conducted in accordance with the same test protocol as that disclosed in "Test Example 1" of Applicants' specification. The *in vivo* test was conducted in

accordance with the same test protocol as that disclosed in "Test Example 2" of Applicants' specification.

The compound defined by amended claim 1 demonstrates a strong DPP-IV inhibitory activity (IC_{50} of 0.25 nM), which is approximately ten times as large as that of the compound of US '969.

As shown in the *in vivo* test results, the compound defined by amended claim 1 shows 100% DPP-IV inhibitory activity, as compared to the compound of US '969, which only shows about 60% DPP-IV inhibitory activity 30 minutes after administration.

Accordingly, the compound claimed in Applicants' amended claim 1 is a superior DPP-IV inhibitor compared with the compound of US '969. As discussed in MPEP 716.02(a)(II), this evidence of superiority in a shared property is enough to rebut an assertion of obviousness.

For these reasons, the invention of independent claim 1, as well as dependent claims 6, 8 and 9 is clearly patentable over the cited references and combinations thereof.

Conclusion

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of objection and rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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